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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,382	09/19/2005	Maria Jose Fernandez		2351

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
03/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,382	FERNANDEZ ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are pending and under consideration in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2-4 require mixing glucomannan with an anionic salt (claim 2), wherein the salt is TPP (claim 3), wherein the TPP is at a concentration of 0.1-5 mg/mL (claim 4).

The specification teaches mixing chitosan, glucomannan and TPP simultaneously. The specification does not provide support for making a solution of glucomannan with TPP and adding glucomannan/TPP to an aqueous chitosan. Literal support for the claim limitations is not found.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term ‘regenerated” in claims 28 and 29 is unclear. To require regeneration infers that the product is lost. The claims are interpreted as thought it reads "reconstituted" in place of "regenerated”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,5-10,12,14-19,21, 23-24,26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Janes (2001, Journal of Controlled Release, 73:255-267).

Janes taught use of chitosan as a pharmaceutically acceptable excipient in formulating and administering doxorubicin. Chitosan is a positively charged carrier attracted to negatively charged cell membranes which was attractive in treating solid tumors. Chitosan was loaded with doxorubicin using TPP to form nanoparticles of 259-292 nm. Janes taught making chitosan nanoparticles using a 0.175% chitosan solution and bring the pH up to 4.7-4.8 with NaOH. Janes used the anionic salt TPP in preparing the particles. Jane also taught using glucomannan as an additional polyanion, incorporating 10% w/w glucomannan in the chitosan/DOX solution. Janes taught lyophilizing the nanoparticles. Claim 27 requires the presence of a cosmetically acceptable excipient. Chitosan is a cosmetically acceptable excipient. Claim 27 fails to require the product be a cosmetic.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 1,5-12,15-21,23-24,26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (2001, Advanced Drug Delivery, 51:81-96) and Illum (1997, Pharmaceutical Research, 11:1186-1189) in view of Wang (2002, International Journal of Pharmaceutics, 244:117-126) and Ryan (2001, Trends in Biotechnology, 19:293-304).

Illum (2001 and 1997) taught use of chitosan as a pharmaceutically acceptable excipient in nasal delivery of vaccines. Illum 1997 taught use of 0.1-1.0% chitosan in solution at pH 4.4 as a carrier for insulin. Chitosan binds strongly to negatively charged materials such as cell surfaces and mucus. Chitosan is able to decrease the clearance of formulations from the nasal cavity and can transiently open tight junctions in mucosal membranes and may lead to an improved immune response. Illum (2001 and 1997) taught use of chitosan particles for the delivery of peptide and protein drugs including insulin (claim 11) and low molecular weight drugs (claim 12). Illum taught that chitosan-based formulations can greatly improve the absorption of drugs. Illum also discuss the use of chitosan in delivery of vaccines including the flu vaccine (2001, see pages 84-85) and the pertussis vaccine (2001, page 86) and diphtheria vaccine (2001, page 88). Illum did not teach physical characteristics of the chitosan particles or addition of glucomannan to the chitosan nanoparticles. Neither Janes nor Illum taught the addition of glucomannan.

However, the use of mannan, specifically glucomannan to target drugs to immune cells was well known in the art. In fact, controlled release beads comprising both chitosan and glucomannan were taught by Wang et al (2002). Wang taught the glucomannan is a water soluble copolymer that had long been known as a drug carrier. Wang taught loading both insulin and BSA on glucomannan particles made from a 0.5% solution. Furthermore, mannan was known to have an advantage in targeting drugs to immune cells. Ryan taught that mucosal delivery of protein antigens are often poorly antigenic. Mannans bind to receptors on macrophages and dendritic cells, which both function as antigen presenting cells.

It would have been obvious to one of skill in the art to combine the teachings regardin use of chitosan in forming nanoparticles for drug or vaccine delivery (Illum) with the teachings that

glucomannan is desirable in targeting proteins, liposomes, and chitosan comprising drugs to immune cells (Wang) to arrive at a glucomannan/chitosan nanoparticle carrying a drug or antigen as claimed. One of skill in the art would have been motivated to make such a combination as the art taught the use of glucomannan in target proteins to immune cells.

The art does not discuss various ratios of glucomannan to chitosan. However, the optimal ratio can be obtained through routine experimentation with each desired bioactive molecule. Wang taught that various glucomannan concentrations could be used and this affected the load and release. In comparing insulin and BSA, two proteins have very different molecular weights, the release of BSA was much lower.

It is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

2) Claims 1,13 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (2001, Advanced Drug Delivery, 51:81-96) and Illum (1997, Pharmaceutical Research, 11:1186-1189) in view of Wang (2002, International Journal of Pharmaceutics, 244:117-126) and Ryan (2001, Trends in Biotechnology, 19:293-304) as applied to claims 1,5-12,15-21,23-24,26 and 27 above, and further in view of Genta (1997, J Pharm Pharmacol, 49:737-742.

Claims 13 and 22 limit the active ingredient to acyclovir or indomethacin.

The teachings of Illum, Wang, and Ryan are set forth above. None of these references taught use of acyclovir or indomethacin as an active ingredient.

However, use of acyclovir in chitosan containing microparticles was known in the art and taught by Genta.

It would have been obvious to replace the active ingredients of chitosan/glucomannan containing nanoparticles with other active ingredients known to work when complexed with chitosan such as acyclovir. One would have been motivated to make such a substitution as the size of nanoparticles is smaller and more able to penetrate mucosa and cell membranes.

It is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

3) Claim 1,13 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janes in view of Genta (1997, J Pharm Pharmacol, 49:737-742).

Claims 13 and 22 limit the active ingredient to acyclovir or indomethacin.

The teachings of Janes are set forth above. None of these references taught use of acyclovir or indomethacin as an active ingredient.

However, use of acyclovir in chitosan containing microparticles was known in the art and taught by Genta.

It would have been obvious to replace the active ingredients of chitosan/glucomannan containing nanoparticles with other active ingredients known to work when complexed with chitosan such as acyclovir. One would have been motivated to make such a substitution as the size of nanoparticles is smaller and more able to penetrate mucosa and cell membranes.

It is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28 and 29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Janes (2001).

The teachings of Janes are set forth above. While Janes did not teach specifically, the addition of water to 'regenerate' the composition, Janes did teach lyophilization, which is dehydration. Before use, it would be obvious to rehydrate the composition using water.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632